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### Multiple autoimmunity in children and young adults type 1 diabetes

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It is well established that individuals with type 1 diabetes (T1D) are at increased risk of other autoimmune diseases but the absolute risks are unclear. The aim of this study was to determine the frequency of autoantibodies to thyroid peroxidase (TPOA), tissue transglutaminase (TgA), and gastric ATPase (ATPase4A) in a well-characterised population based cohort with T1D and to identify the genetic characteristics of multiple autoimmunity.

Samples were analysed from individuals with T1D [n=1061; 464 male; median age 11.8yrs (range 0.7-28yrs), median age at diagnosis 10.9 yrs (range 0.4-21yrs)] participating in the population-based Bart's Oxford (BOX) family study. Autoantibodies to TPO, Tg and ATPase were measured by radioimmunoassay. HLA class II and non-HLA SNPs (rs3087243 in CTLA-4, rs12935413 in KIAA0350 and rs1893217 in PTPN2) analysis was carried out by PCR-SSP and Taqman genotyping respectively.

Overall, 22.7% of individuals with T1D were positive for at least one non-islet autoantibody. The prevalence of TPOA, TgA and ATPase4A in patients was 9.2%, 9.1%, and 8.4% respectively. Two autoantibodies were observed in 2.8% and all three autoantibodies in 0.3% of the cohort. TgA was associated with younger age and TPOA with older age ( $p < 0.001$  for both) but no age effect was observed for ATPase4A. All autoantibodies were associated with female gender ( $p < 0.005$ ). Risk of multiple autoimmunity is modulated by different HLA class II DRB1\*03,\*04 and non-HLA SNP combinations.

Over one fifth of children with T1D will develop gut, thyroid or gastric autoimmunity. HLA and non-HLA genes modulate risk, supporting evidence for common pathways of autoimmunity.